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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,884	10/15/2003	Jennifer L. Harris	18062G-003211US	7551

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,884	HARRIS ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *84-114* is/are pending in the application.

4a) Of the above claim(s) *91-114* is/are withdrawn from consideration.

5)☒ Claim(s) *90* is/are allowed.

6)☒ Claim(s) *84-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-final rejection filed on January 23, 2008 is acknowledged. Claims 84-114 are pending in this application. Applicant elected with traverse Group I (claims 84-90) drawn to a material having a fluorogenic moiety linked to a solid support and the species election wherein R^{15} is an amine protecting group in the reply filed on May 30, 2007. The restriction requirement was deemed proper and made FINAL in the previous office action. Claims 91-114 remain withdrawn from further consideration. Claims 84-90 are examined on the merits in this office action.

Extension of three months time filed on January 23, 2008 is acknowledged.

Withdrawn Objection

1. The objection to the title being too long is hereby withdrawn due to Applicant's amendment of the title to "Fluorogenic Materials and Uses Thereof".

2. The objection to the abstract is hereby withdrawn due to Applicant's amendment to the abstract.

Maintained Rejection

35 U.S.C. 112, 1st

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 84 and 87-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

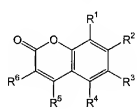
5. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

6. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

7. The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

8. In the instant case, the claims are drawn to a material having a fluorogenic



moiety linked to a solid support, the material having the structure

wherein R^1, R^3, R^4 and R^6 are each H, R^2 is NHR^{15}, and R^5 is $-R^{14}$-SS wherein R^{14} is --

$CH_2C(O)NH$--, R^{15} is a member selected from the group consisting of amine protecting groups, -C(O)-AA and –C(O)-P. The generic statements R^{15} is a member selected from the group consisting of -C(O)-AA and –C(O)-P do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

9. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 84 is broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of amino acid or peptide or a peptide-like molecule that can form peptide bonds. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a

peptide-like molecule or other peptidic molecules and other synthetic peptide or peptide-like molecule that can form peptide bonds.

10. The specification is limited to the amino acid residues consisting of natural amino acids, unnatural amino acids and modified amino acids (see paragraph [0076). The specification discloses that P is a peptide sequence comprising the structure –C(O)-AA^1-AA^2-$(AA^i)_{J-2}$, and AA^1 through AA^i is an amino acid residue which is a member independently selected from the group of natural amino acid residues, unnatural amino acid residues and modified amino acid residues, J denotes the number of amino acid residues forming the peptide sequence and is a member selected from the group consisting of the numbers from 2 to 10, such that J-2 is the number of amino acid residues in the peptide sequence exclusive of an amino acid residue relevant to AA^1, and when J is greater than 2, i is a member selected from the group consisting of the numbers from 3 to 10 (see paragraph [0074]). The specification does not describe any examples of –C(O)-AA or -C(O)-P at R^{15}. Description of peptide libraries wherein P1 is fixed and having P1-P4 is not sufficient to encompass numerous other amino acids and peptides and proteins that belong to the same genus. For example, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus. As disclosed in the specification, amino acid residues consist of natural amino acids, unnatural amino acids and modified amino acids. There are 20 naturally occurring amino acids, and there are unnatural amino acids (such as D-amino acids of the naturally occurring amino acids, β-amino acids, γ-amino acids, ε-amino acids), synthetic amino acids, amino acid mimetics and modified amino acids such as

methylated Phe. There are innumerable possibilities of what the single amino acid residue can encompass. With the case where in R^{15} is –C(O)-P, since the peptide can be AA^1-AA^2-$(AA^i)_{J-2}$, and AA^1 through AA^i is an amino acid residue which is a member independently selected from the group of natural amino acid residues, unnatural amino acid residues and modified amino acid residues, J denotes the number of amino acid residues forming the peptide sequence and is a member selected from the group consisting of the numbers from 2 to 10, such that J-2 is the number of amino acid residues in the peptide sequence exclusive of an amino acid residue relevant to AA^1, and when J is greater than 2, i is a member selected from the group consisting of the numbers from 3 to 10, this peptide can encompass any vast number of different peptide content. As described above, there are 20 naturally occurring amino acids, and there are unnatural amino acids (such as D-amino acids of the naturally occurring amino acids, β-amino acids, γ-amino acids, ε-amino acids), synthetic amino acids, amino acid mimetics and modified amino acids such as methylated Phe. There are innumerable possibilities of what the single amino acid residue can encompass, thus, there is innumerable possibilities of peptide and different combination of amino acid residues. Thus, there is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

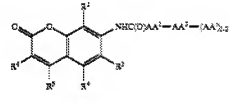
11. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals

appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Applicant's Arguments

12. Applicant argues that "it is well-settled that the disclosure of a single species may support a genus." Applicant argues that "those of skill in the art would clearly understand that the phrase 'R^{15} is a member selected from the group consisting of –C(O)-AA and –C(O)-PP' is intended to mean that either (i) a single amino acid or (ii) a peptide sequence is covalently coupled, i.e., attached, to the fluorogenic moiety set forth in claim 84." Applicant further argues that "with respect to [peptide sequence] latter, however, the specification provides additional information regarding the meaning of this term, and importantly, provides a more detailed definition of this term…the specification provides explicit information regarding the structure of the polypeptide sequence." Further, Applicant argues that "the description of these common features in both the specification and claims provides more than adequate written description for the claimed invention."

Applicant argues that "the specification does provide examples of the presently claimed fluorogenic materials and details methods for preparing such fluorogenic materials."

13. Applicant's arguments have been fully considered but have not been found persuasive because Applicant only had possession of fluorogenic moiety that had tetrameric peptide conjugated. In regards to MPEP 2163 that states, "What constitute a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed", the species in question are the peptide sequences conjugated to the fluorogenic moiety. The specification discloses  .

And as described above, AA^1 through AA^I is an amino acid residue which is a member independently selected from the group of natural amino acid residues, unnatural amino acid residues and modified amino acid residues, J denotes the number of amino acid residues forming the peptide sequence and is a member selected from the group consisting of the numbers from 2 to 10, such that J-2 is the number of amino acid residues in the peptide sequence exclusive of an amino acid residue relevant to AA^1, and when J is greater than 2, i is a member selected from the group consisting of the numbers from 3 to 10. Therefore, for example, if J is 10, then J-2 is 8, and therefore the peptide sequence will be AA^1-AA^2-AA^3-AA^4-AA^5-AA^6-AA^7-AA^8-AA^9-AA^{10}. Since the specification discloses that amino acid residue is a member independently selected from the group consisting of natural amino acid residues, unnatural amino acid residues

and modified amino acid residues (see paragraph [0015]), this implies that there are 10^{20}= $1X10^{20}$ possible peptide sequences for naturally occurring amino acid residues. When unnatural amino acids and modified amino acids are factored into the equation, then there are innumerable numbers of possible peptide sequences. Applicant has directed the Examiner to the examples. However, most of the examples describe a tetramer peptide sequences (see for example, see FIG.1, Tables II and III, and SEQ ID NOS: 1-11). Description of tetramers is not enough to encompass the whole peptide genus claimed. Thus, there is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

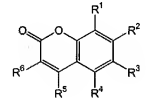
Obviousness Double Patenting

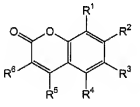
14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 84-88 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,680,178. Although the conflicting claims are not identical, they are not patentably distinct from each other because if one practiced the claimed invention of the instant claims, one would achieve the claimed invention of U.S. Patent No. 6,680,178 and vice versa.

16. The instant claims are drawn to a material having a fluorogenic moiety linked to a solid support, the material having the structure  wherein R^1, R^3, R^4 and R^6 are each H; R^2 is NHR^{15}, and R^5 is $–R^{14}$-SS, wherein R^{14} is $–CH_2C(O)NH$-, R^{15} is amine protecting groups, -C(O)-AA and –C(O)-P.

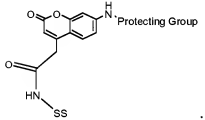
17. U.S. Patent No. 6,680,178 claims are drawn to a material having a fluorogenic moiety linked to a solid support, said material having the structure  wherein R^1, R^2, R^3, R^4, R^5 and R^6 are independently selected from the group consisting of H, halogen, $-NO_2$, -CN, $-C(O)_mR^7$, $-C(O)NR^8R^9$, $-S(O)_tR^{10}$, $-SO_2NR^{11}R^{12}$, $-OR^{13}$, substituted or unsubstituted alkyl, $-R^{14}$-SS, and $–NHR^{15}$ with a proviso that at least one of R^1, R^2, R^3, R^4, R^5 and R^6 is $–R^{14}$-SS and at least one or R^1, R^2, R^3, R^4, R^5 and R^6 is $–NHR^{15}$, R^{14} is a linking group, R^{15} is $–CH_2C(O)NH$-, R^{15} is amine protecting groups, -C(O)-AA and –C(O)-P.

18. Therefore, the instant claims are drawn to the material having a fluorogenic moiety linked to a solid support, wherein R^1, R^3, R^4 and R^6 are each H; R^2 is NHR^{15}, and R^5 is $-R^{14}$-SS, wherein R^{14} is $-CH_2C(O)NH-$, R^{15} is amine protecting groups, -C(O)-AA and –C(O)-P, one of the species of the U.S. Patent No. '178. Therefore, if one practiced the claimed invention of the instant claims, one would necessarily achieve the claimed invention of the U.S Patent No. '178 and vice versa.

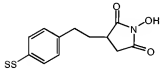
Conclusion

Allowable Subject Matter

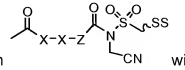
18. Claim 90 is allowable. Claims 84-89 are rejected. The claims are drawn to a material having a fluorogenic moiety linked to a solid support having the structure



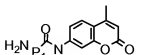
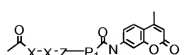
. Support bound fluorogenic materials are known in the art:

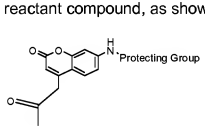


(see for example, Adamczyk et al, Bioorganic & Medicinal Chemistry Letters, 1999, 9: 217-220). The closest art found was Backes et al (Nature Biotechnology, 2000, 187-193). Backes et al teach



with the solid

support reacting with  to form  . Backes et al does not teach a solid support structure bound to the structure  on the 6th carbon of the ring structure and does not teach a amine group protected with a protecting group on the carbon at position 2 on the ring. It would not be obvious to attach a solid support from the amine group coming off of the carbon at position 6. There are other sites that can have solid support attached to, such as the NH bonded to carbon at position 2, or any other sites that has a free amine or free carbon group, as shown by Adamczyk et al above. Furthermore, solid support can be attached to the reactant compound, as shown by Backes et al above. Thus, the invention structure



is both novel and unobvious over the prior arts.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Examiner, Art Unit 1654

/Anish Gupta/
Primary Examiner, Art Unit 1654